

NCI Thesaurus Drug/Agent Modeling Samples

3/8/04

Imatinib

Definition A Bcr-Abl tyrosine kinase inhibitor which interferes with intracellular signaling pathways, resulting in decreased proliferation and induction of apoptosis in Bcr-Abl positive cell lines and leukemic cells from Philadelphia chromosome positive myeloid leukemia.

CD_Has_MOA	Tyrosine Kinase Inhibition
CD_Has_PE	Cell Signal Transduction Inhibition Cell Proliferation Inhibition Apoptosis Induction
CD_Metabolized_By_Enzyme	Cytochrome P450 3A4
CD_Affects_Gene_Product	Bcr/abl Oncoprotein Stem Cell Factor Receptor Platelet-derived Growth Factor Receptor Abl2 Tyrosine Kinase
CD_Has_Accepted_Therapeutic_Use	Gastrointestinal Stromal Tumor (GIST) Chronic Myeloid Leukemia
CD_Has_Study_Therapeutic_Use	Extensive Stage Small Cell Lung Cancer, Bcr/Abl Positive Hematological Malignancies, Advanced Malignancies with Liver Dysfunction, Recurrent Malignant Glioma or Meningioma, Acute Lymphoblastic Leukemia, Metastatic Melanoma, Metastatic Breast Cancer, Unresected Merkel Cell Carcinoma, Stage III/IV Ovarian Epithelial or Primary Peritoneal Cancer, Recurrent Ewings Family Tumors or Desmoplastic Small Round-Cell Tumor, Metastatic and/or Unresectable Adenocarcinoma of the Stomach, Relapsed or Refractory Pediatric Solid Tumors, Stage IV Colorectal Cancer expressing c-kit, Arg, Abl, or PDGF-R

Trastuzumab

Definition A humanized recombinant monoclonal antibody directed against the HER2-receptor protein. Trastuzumab binds to the extracellular domain of the growth factor protein HER2, thereby inhibiting proliferation of HER2 overexpressing tumor

cells. Binding with HER2 protein also initiates an antibody-dependent cell cytotoxicity.

CD_Has_MOA	Receptor Tyrosine Kinase Inhibition
CD_Has_PE	Cell Signal Transduction Inhibition Cell Proliferation Inhibition Cytolysis Induction
CD_Affects_Gene_Product	ERBB2 Receptor Protein-Tyrosine Kinase
CD_Has_Accepted_Therapeutic_Use	Breast cancer overexpressing HER2 protein Pancreatic cancer overexpressing p185HER2
CD_Has_Study_Therapeutic_Use	Breast cancer, metastatic osteosarcoma, solid tumors, brain metastases secondary to lung cancer, HER2/neu-overexpressing malignancies

Bizelesin

Definition A synthetic cyclopropylpyrroloindole antineoplastic antibiotic that binds to the minor groove of DNA and induces interstrand cross-linking of DNA, thereby inhibiting DNA replication and RNA synthesis. Bizelesin enhances p53 and p21 induction and triggers G2/M cell-cycle arrest, resulting in cell senescence without apoptosis.

CD_Has_MOA	DNA Minor Groove Binding Interaction DNA Crosslinking Interaction
CD_Has_PE	DNA Replication Inhibition RNA Synthesis Inhibition G2 to M Phase Arrest Cell Senescence Induction
CD_Affects_Gene_Product	Tumor Protein p53 Cyclin-Dependent Kinase Inhibitor 1A p21 K-Ras protein
CD_Has_Accepted_Therapeutic_Use	None current
CD_Has_Study_Therapeutic_Use	None current

